

substance that favourably affects heart failure, either in a free combination or in a fixed combination in a tablet. A therapeutically effective dose of the DPP IV inhibitor (e.g. a dose of between 0.1 and 100 mg) may be combined with different doses of ACE-inhibitors (e.g. 2.5 mg to 15 mg ramipril), AT1-receptor-antagonists (e.g. 20 mg to 160 mg telmisartan), beta-blockers (e.g. 50 mg to 200 mg metoprolol), combined alpha/beta-blockers (e.g. 3.25 mg to 100 mg carvedilol), diuretics (e.g. 12.5 mg to 25 mg hydrochlorothiazide), mineralocorticoid receptor antagonists (e.g. 25 mg to 100 mg eplerenone; and/or B-type natriuretic peptide (BNP) (e.g. 2 µg/kg as a bolus followed by 0.01 µg/kg/min nesiritide), a BNP-derived peptide or a BNP-fusion product. The combination of BNP and DPP-IV inhibitor leads to a higher concentration of full length BNP (1-32) in vivo. The clinical efficacy of the combinations specified can be tested in clinical studies. The treatment lasts between 1 day and 6 years. Evidence that the combination is effective in treating acute heart failure can be found in the fact that compared with other therapies the combination leads to a significant improvement in the clinical situation (higher cardiac ejection output and/or reversal of pulmonary congestion, and/or reversal of pulmonary wedge pressure, and/or a reduction in mortality caused by acute heart failure).

Example 19

Treatment with DPP-IV Inhibitor in Patients with Heart Failure

A DPP IV inhibitor according to the invention may be used to treat a patient with chronic heart failure. This treatment leads to a higher concentration of endogenous full length BNP (1-32) in vivo. The clinical efficacy of this treatment is tested in clinical studies. The treatment lasts between 2 weeks and 6 years. Evidence that the combination is effective in treating chronic heart failure can be found in the fact that a DPP-IV inhibitor according to the invention leads to a significant improvement in the clinical situation compared with a different treatment or placebo (less frequent hospitalisation due to acute heart failure, the ability to walk longer distances, a higher loadability in ergometrics, a higher cardiac ejection output and/or reversal of pulmonary congestion, and/or a reduction in mortality caused by heart failure).

What is claimed is:

1. A method of treating type II diabetes mellitus comprising administering to a patient in need thereof a pharmaceutically effective oral amount of 1-[(4-methyl-quinazolin-2-yl)-methyl]-3-methyl-7-(2-butyn-1-yl)-8-(3-(R)-amino-piperidin-1-yl)-xanthine, and a pharmaceutically effective amount of metformin, which is from 300 mg to 1000 mg once or twice a day, or delayed-release metformin in a dose of 500 mg to 1000 mg once or twice a day or 500 mg to 2000 mg once a day.

2. The method according to claim 1, wherein the pharmaceutically effective oral amount of 1-[(4-methyl-quinazolin-2-yl)-methyl]-3-methyl-7-(2-butyn-1-yl)-8-(3-(R)-amino-piperidin-1-yl)-xanthine is an oral daily dose of from 2.5 mg to 10 mg.

3. The method according to claim 1, wherein the 1-[(4-methyl-quinazolin-2-yl)-methyl]-3-methyl-7-(2-butyn-1-yl)-8-(3-(R)-amino-piperidin-1-yl)-xanthine is administered in an oral dosage of from 0.5 mg to 50 mg.

4. The method according to claim 1, wherein the 1-[(4-methyl-quinazolin-2-yl)-methyl]-3-methyl-7-(2-butyn-1-yl)-8-(3-(R)-amino-piperidin-1-yl)-xanthine is administered in an oral dosage of from 2.5 mg to 10 mg.

5. The method according to claim 1, wherein the 1-[(4-methyl-quinazolin-2-yl)-methyl]-3-methyl-7-(2-butyn-1-yl)-8-(3-(R)-amino-piperidin-1-yl)-xanthine is administered in an oral dosage of 0.5 mg, 1 mg, 2.5 mg, 5 mg or 10 mg.

6. The method according to claim 1, wherein the 1-[(4-methyl-quinazolin-2-yl)-methyl]-3-methyl-7-(2-butyn-1-yl)-8-(3-(R)-amino-piperidin-1-yl)-xanthine is administered in an oral dosage of 1 mg, 2.5 mg or 5 mg.

7. The method according to claim 1, wherein the 1-[(4-methyl-quinazolin-2-yl)-methyl]-3-methyl-7-(2-butyn-1-yl)-8-(3-(R)-amino-piperidin-1-yl)-xanthine is administered in an oral dosage of 2.5 mg or 5 mg.

8. The method according to claim 1, wherein the 1-[(4-methyl-quinazolin-2-yl)-methyl]-3-methyl-7-(2-butyn-1-yl)-8-(3-(R)-amino-piperidin-1-yl)-xanthine is administered in an oral dosage of from 2.5 mg to 50 mg.

9. The method according to claim 1, wherein the 1-[(4-methyl-quinazolin-2-yl)-methyl]-3-methyl-7-(2-butyn-1-yl)-8-(3-(R)-amino-piperidin-1-yl)-xanthine is administered in an oral daily dose of 5 mg.

10. A method of treating type 2 diabetes or pre-diabetes comprising administering to a patient in need thereof a therapeutically effective oral dose of 1-[(4-methyl-quinazolin-2-yl)-methyl]-3-methyl-7-(2-butyn-1-yl)-8-(3-(R)-amino-piperidin-1-yl)-xanthine in combination with a therapeutically effective dose of metformin, which is 500 mg, 850 mg or 1000 mg metformin as a single dose with a total daily dose of metformin of 500-2850 mg, or which is 500 mg, 1000 mg, 1500 mg or 2000 mg metformin in delayed release form.

11. The method according to claim 10, wherein the 1-[(4-methyl-quinazolin-2-yl)-methyl]-3-methyl-7-(2-butyn-1-yl)-8-(3-(R)-amino-piperidin-1-yl)-xanthine is administered in an oral dosage of from 0.5 mg to 50 mg.

12. The method according to claim 10, wherein the 1-[(4-methyl-quinazolin-2-yl)-methyl]-3-methyl-7-(2-butyn-1-yl)-8-(3-(R)-amino-piperidin-1-yl)-xanthine is administered in an oral dosage of from 2.5 mg to 10 mg.

13. The method according to claim 10, wherein the 1-[(4-methyl-quinazolin-2-yl)-methyl]-3-methyl-7-(2-butyn-1-yl)-8-(3-(R)-amino-piperidin-1-yl)-xanthine is administered in an oral dosage of 0.5 mg, 1 mg, 2.5 mg, 5 mg or 10 mg.

14. The method according to claim 10, wherein the 1-[(4-methyl-quinazolin-2-yl)-methyl]-3-methyl-7-(2-butyn-1-yl)-8-(3-(R)-amino-piperidin-1-yl)-xanthine is administered in an oral dosage of 1 mg, 2.5 mg or 5 mg.

15. The method according to claim 10, wherein the 1-[(4-methyl-quinazolin-2-yl)-methyl]-3-methyl-7-(2-butyn-1-yl)-8-(3-(R)-amino-piperidin-1-yl)-xanthine is administered in an oral dosage of 2.5 mg or 5 mg.

16. The method according to claim 10, wherein the 1-[(4-methyl-quinazolin-2-yl)-methyl]-3-methyl-7-(2-butyn-1-yl)-8-(3-(R)-amino-piperidin-1-yl)-xanthine is administered in an oral dosage of from 2.5 mg to 50 mg.

17. The method according to claim 10, wherein the 1-[(4-methyl-quinazolin-2-yl)-methyl]-3-methyl-7-(2-butyn-1-yl)-8-(3-(R)-amino-piperidin-1-yl)-xanthine is administered in an oral daily dose of 5 mg.

18. A method of treating type II diabetes mellitus comprising administering to a patient in need thereof a pharmaceutically effective oral amount of 1-[(4-methyl-quinazolin-2-yl)-methyl]-3-methyl-7-(2-butyn-1-yl)-8-(3-(R)-amino-piperidin-1-yl)-xanthine which is an oral daily dose of from 2.5 mg to 10 mg, and a pharmaceutically effective amount of metformin.

19. A method of treating type II diabetes mellitus comprising administering to a patient in need thereof a pharmaceutically effective oral amount of 1-[(4-methyl-quinazolin-2-yl)-